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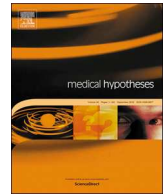
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# Pre-operative rehabilitation in lower-limb amputation patients and its effect on post-operative outcomes

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## ABSTRACT

Major lower-limb amputation (LLA) is a life-changing event associated with poor post-operative physical and psychological functioning and decreased quality of life. The general physical condition of most LLA patients prior to surgery is already significantly deteriorated due to chronic peripheral vascular disease often in combination with diabetes. Pre-operative rehabilitation (also called 'pre-rehabilitation') is an increasingly common strategy used in multiple patient populations to improve patients' physical and mental condition prior to surgery, thus aiming at improving the post-operative patient outcomes. Given the positive effects of post-surgical outcomes in many patient populations, we hypothesize that pre-operative rehabilitation will improve post-operative outcomes after LLA.

To test this hypothesis, a literature search of PubMed, EMBASE, EBSCOhost, Web of Science and ScienceDirect was performed to identify studies that investigated the impact of a pre-operative rehabilitation therapy on post-operative outcomes such as length of hospital stay, mobility, physical functioning, and health related quality of life. No time restrictions were applied to the search. Only articles published in English were included in the selection. Two studies satisfied the eligibility criteria for inclusion in the review, one qualitative and one quantitative study. The quantitative study reported a beneficial effect of pre-rehabilitation, resulting in post-operative mobility (at least indoor ambulation) in 63% of the included LLA patients. There is a need for prospective clinical studies examining the effect of pre-rehabilitation on post-operative outcomes to be able to confirm or reject our hypothesis. Although the hypothesis seems plausible, evidence is lacking to support our hypothesis that pre-operative rehabilitation will improve post-operative outcomes in patients with LLA. The qualitative study indicated that integrating pre-rehabilitation in the care for LLA patients seems to be limited to a selected group of dysvascular patients, but at this stage cannot be advised based on current evidence even in this subgroup. Further research is needed to clarify whether such an intervention prior to amputation would be a useful and effective tool for optimizing post-operative outcomes in LLA patients.

## Background

A major lower-limb amputation (LLA) is a drastic life-changing event which, in most cases, results in a poor post-operative physical and psychological condition, permanent disability and decreased quality of life [1]. The most common causes of LLAs worldwide are peripheral vascular disease (PVD), diabetes mellitus, severe trauma, neoplasia, infection and congenital defects [2–4]. In the Netherlands, LLAs are performed mainly due to PVD with critical ischemia combined with diabetes mellitus in overwhelming majority of the cases [5]. The amputation level is an important determinant of the patient's mobility and physical functioning post-operatively, therefore decisions related to surgical interventions at a specific anatomical lower limb level are of

extreme importance for the patient's rehabilitation process and post-operative outcomes [6].

In order to be able to walk again after surgery, a LLA patient needs a prosthesis which requires great energy expenditure; so maintaining good physical fitness is the key to tolerating the increased energy demand [7]. However, the pre- and post-operative physical condition of LLA patients generally tends to be low because of existing co-morbidities such as diabetes mellitus and PVD which are usually also the main causes leading to the amputation [1]. Increased age and possibly reduced motivation to maintain good physical fitness could also be important factors influencing the physical abilities and functional outcomes of LLA patients post-operatively [8]. Therefore, there is an increased need for dedicated cardiovascular and muscular strength

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exercise programs in these patients aiming at improving their physical fitness prior to amputation, which would possibly result in improved post-operative physical and psychological functioning, thus leading also to a general improvement in the health related quality of life (HRQoL) of the patient.

Pre-operative physical rehabilitation, also called ‘pre-rehabilitation’, has been increasingly used in various patient groups in order to improve post-operative outcomes such as functional capacity, length of hospital stay (LOS) and possible peri- and post-operative complications [9,10]. Pre-rehabilitation is the process of enhancing and optimizing one’s physical fitness with the aim to enable them to withstand a stressful surgical event associated with inactivity [11]. Such a pre-rehabilitation program usually commences 4–6 weeks prior to surgery and comprises of repetitive physical exercises preferably combined with occupational therapy, psychosocial assessment and education regarding the rehabilitation experience and possible prosthetic fitting post-operatively [12–16]. It was suggested that a pre-operative program used in the treatment of young LLA patients consists of chest physiotherapy, muscle and joint mobility training, focusing on strength and function preservation [3]. Also general muscle strengthening interventions can be initiated prior to surgery in order to enable prospective LLA patients to be independent and more mobile during their post-operative period [17]. The need for maintaining mobility, activity and good range of motion (ROM) of the unaffected limbs, cardiopulmonary conditioning including dynamic exercises as tolerated, as well as psychosocial interventions are emphasized so that the patient achieves maximal functional fitness and adapts psychologically and emotionally to the amputation in the pre- and post-operative rehabilitation period [12,14,18]. In order to standardize and improve rehabilitation care of LLA patients, the Department of Veterans Affairs (VA) and the Department of Defense (DoD), USA, published guidelines in 2017 which give a thorough elucidation of all rehabilitation phases starting with pre-operative care [19]. The Dutch guidelines published in 2012 provide a structured evidence-based approach for the rehabilitation period of patients awaiting for LLA [5]. However, pre-operative rehabilitation interventions are not described in these guidelines.

The effectiveness of pre-rehabilitation has been demonstrated in multiple patient groups. For example, patients undergoing cardiovascular and abdominal surgery showed improved muscle function shorter hospital stay and reduced postoperative complication after a pre-rehabilitation program [9,20–26]. Additionally, there is evidence in the literature that pre-operative rehabilitation in patients undergoing hip and knee arthroplasty contributes to decreased LOS [26]. A few studies examining pre-operative rehabilitation in lung cancer patients who undergo lung resection also demonstrate that pulmonary rehabilitation prior to surgery results in improved exercise capacity and decreased LOS after surgery [27–29]. Beneficial effects of active participation in rehabilitation and physical therapy before surgery have also been reported in liver transplantation patients on a liver transplant waiting list, whose significantly reduced pre-operative functional status (including disease-associated fatigue, muscle wasting, and ascites) usually results in inactivity or immobility [30]. Pre-transplant rehabilitation and conditioning has also been demonstrated to improve transplant candidacy, speed up the recovery process, improve post-operative exercise capacity and muscle strength, and contribute to both decreased intensive care unit and hospital LOS following lung transplantation [31,32].

**Hypothesis.** *The findings retrieved from the current literature indicate that pre-rehabilitation interventions in LLA patients is thought to be useful and effective with respect to post-operative outcomes such as mobility, LOS, HRQoL, post-operative recovery including possible complications, morbidity and survival. Hence, we hypothesize that, given the positive effects of post-surgical outcomes in many patient populations, pre-operative rehabilitation*

*will improve post-operative outcomes after LLA.*

## Methods

To test the hypothesis a review of literature was performed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [33].

## Eligibility criteria

Studies have been selected on the basis of specific inclusion and exclusion criteria which were the same for the three phases of selection, being title, abstract and full-text selection processes. Inclusion criteria were: primary research, target population of at least five LLA patients, focus on pre-operative physical or psychosocial interventions/care, for instance physical therapy, exercise, physical conditioning, or psychotherapy. Next to that, studies had to specify post-operative outcomes such as physical functioning, mobility, LOS and recovery time, HRQoL, or complication rates, in order to be accepted for next phase selection. Only articles published in English were included in the selection. No time restrictions were applied to the literature search.

Articles were excluded when they only focused on post-operative interventions such as post-operative rehabilitation alone and prosthesis fitting. Articles that involved other surgical interventions than LLA were also excluded. Lastly, reviews, case studies, comments, interviews, letters, posters, books and book chapters were excluded. If, after title and abstract evaluation, the inclusion or exclusion of an article was still uncertain, the article was included in the next selection phase.

## Information sources and search strategy

The following five databases were searched for the purposes of this systematic review: PubMed, EMBASE, EBSCOhost, Web of Science and ScienceDirect. The search strategy used included a combination of database-specific MeSH terms, Boolean operators (“AND”, “OR” or “NOT”) to combine search terms, free text words and ‘wild cards’ (using truncation character “\*”). The complete search strategy details for each database are presented under Appendix 1. The main key words for the search included “preoperative care”, “preoperative rehabilitation”, “prehabilitation”, “preoperative training”, “preoperative therapy”, “preoperative service”, “preoperative exercise”, “pre-operative physical therapy” and “pre-operative intervention” in combination with “lower limb”, “lower extremity”, “amputation” and “amputees”. Duplicates from all five databases were removed. Manual searches were conducted as well. The most recent search date was February 24th 2020.

## Study selection

Two reviewers assessed titles, abstracts, and full texts independently. A consensus meeting was held after every stage to ensure that comparison is made between individual results, and agreements on differences in assessment are achieved. If consensus between the two reviewers was not met in a certain stage, a third reviewer made the final decision regarding the eligibility of the particular article. After the full-text selection phase, both reviewers used a quality assessment checklist to evaluate the methodological quality and internal validity of the included articles (see Appendix 2). References of papers selected for the final assessment phase of the review were checked for relevant citations as well.

## Data extraction

In order to support or reject our hypothesis, data was extracted from the included quantitative studies. The data extracted from the selected studies were general study information, number of patients, and patient characteristics. General study information included authors, year of publication, duration of study, patient population, post-operative outcomes, outcome measurement tool, type of pre-operative rehabilitation intervention, its frequency, intensity, and duration, as well as inclusion/exclusion criteria within each study. In terms of patient characteristics, median age, level of amputation, reason for amputation, as well as percentage of males and females included in the study were recorded. The post-operative outcomes of interest such as physical functioning, mobility, LOS and recovery time, HRQoL, and complication rates were extracted.

## Risk of bias assessment

The tool used for assessing risk of bias in individual quantitative studies is A Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI) [31]. It covers seven domains through which different types of bias might be introduced into a Non-Randomized Study (NRS), namely bias due to confounding, bias in selection of participants into the study, bias in measurement of interventions, bias due to departures from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported result.

## Data analysis

Analysis of the data could not be undertaken due to the fact that only one quantitative study and one qualitative study met the inclusion criteria and were subsequently included in the review after the full-text selection stage. The results are therefore presented as a narrative analysis of the data from this study.

## Results

### Study selection

The search of PubMed, EBSCOhost, Embase, ScienceDirect and Web of Science provided a total of 217 articles after duplicates were removed. After the evaluation of the titles, 69 records were included for further selection. The review of the abstracts resulted in the selection of 21 articles meeting the inclusion criteria and were included for full text assessment. The 48 discarded articles clearly did not meet the inclusion criteria. These articles concern no primary research or are not focused either on post-operative rehabilitation alone or on pre-operative assessment not involving the actual implementation of a pre-rehabilitation program. Checking the references of the articles selected for the full text phase did not lead to any additional articles to be included. After assessing the full texts, two studies met the inclusion criteria and were, therefore, included in the systematic review for further analysis. One of the studies was a qualitative study, and one was a quantitative. Nineteen articles in total have been excluded since they fell outside the eligibility criteria. Fifteen articles were not scientific studies (no primary research), instead these papers provided step-by-step description of the pre- and post-operative rehab phases, like pre and post-rehabilitation guidelines, without any proof of effectiveness and four papers only reported the odds of receiving preoperative therapy without reporting outcomes. Every step of the whole article selection process is illustrated in Fig. 1 which shows the PRISMA Flow Diagram of the literature search [33].

## Risk of bias within study

One of the included studies was assessed for risk of bias, as only quantitative studies were assessed. The Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI) [34] based on seven domains was used. Within-study risk of bias is presented in Table 1. The significant lack of information provided in the article represented an obstacle for the proper assessment of the risk of bias within the included study. The study did not elaborate on an explanation of the contents of the pre-operative intervention such as specific exercises, exact duration, frequency and intensity and lacked a clear presentation and explanation of the statistical analysis of the patient outcomes. Therefore, the judgment of the risk of bias of the study turned out to be quite burdensome and resulted in an overall high or unclear risk of various types of bias assessed by the risk of bias assessment tool.

## Characteristics of the study population

The 2-year quantitative study of Turney et al. [35] which fulfilled all eligibility criteria for final selection, included a total of 87 major LLA patients with median age of 74 years. The patient group comprised of 60 men and 27 women, representing 69% and 31% of the whole patient group respectively. The number of drop-outs was 21, 12 of whom died in the *peri*-operative period (i.e. before being discharged from hospital), and a further 9 patients died over the 2-year period of the study. A summary of the study information is provided in Table 2.

The patients included in the study underwent different levels of amputation: 43 had unilateral below knee amputations (BKA), 27 had unilateral above knee amputations (AKA), and two had hip disarticulations. There were 15 bilateral amputation patients, 11 of whom with a bilateral BKA, two patients with one BKA and one AKA, and two patients with bilateral AKAs. The main reason for the majority of amputations (70) was critical ischemia, whereas the remainder (17) were performed for a variety of orthopedic, ulcerative, and oncological reasons. The study characteristics of the included study are described in Table 3.

## Assessment method

To assess post-operative mobility in LLA patients, the study of Turney et al. used the Wood/Stammore scale [35]. This scale was used by the physiotherapists to score the predicted and maximum achieved mobility of each patient after amputation. It assesses both household and community ambulatory mobility. It is a 5 point scale ranging from cosmetic use of a prosthesis (1) to independent outdoor mobility (5). No published evidence of testing for validity or reliability is available [36].

## Pre-operative exercise intervention

Daily physiotherapy was initiated before the amputation for patients with any mobility, or any potential for mobility. The rehabilitation team consisted of vascular surgeons, rehabilitation physicians, physiotherapists and occupational therapists. The authors, however, did not provide any information regarding the exact components of the pre-operative intervention such as specific physical exercises, intensity, and duration.

## Post-operative outcomes

The outcome of interest of the study was the post-operative mobility of LLA patients [35]. Twenty one patients died during the course of the study, which resulted in 66 patients who continued with their participation in the study. Mobility (a score of 3 or higher on the Wood/

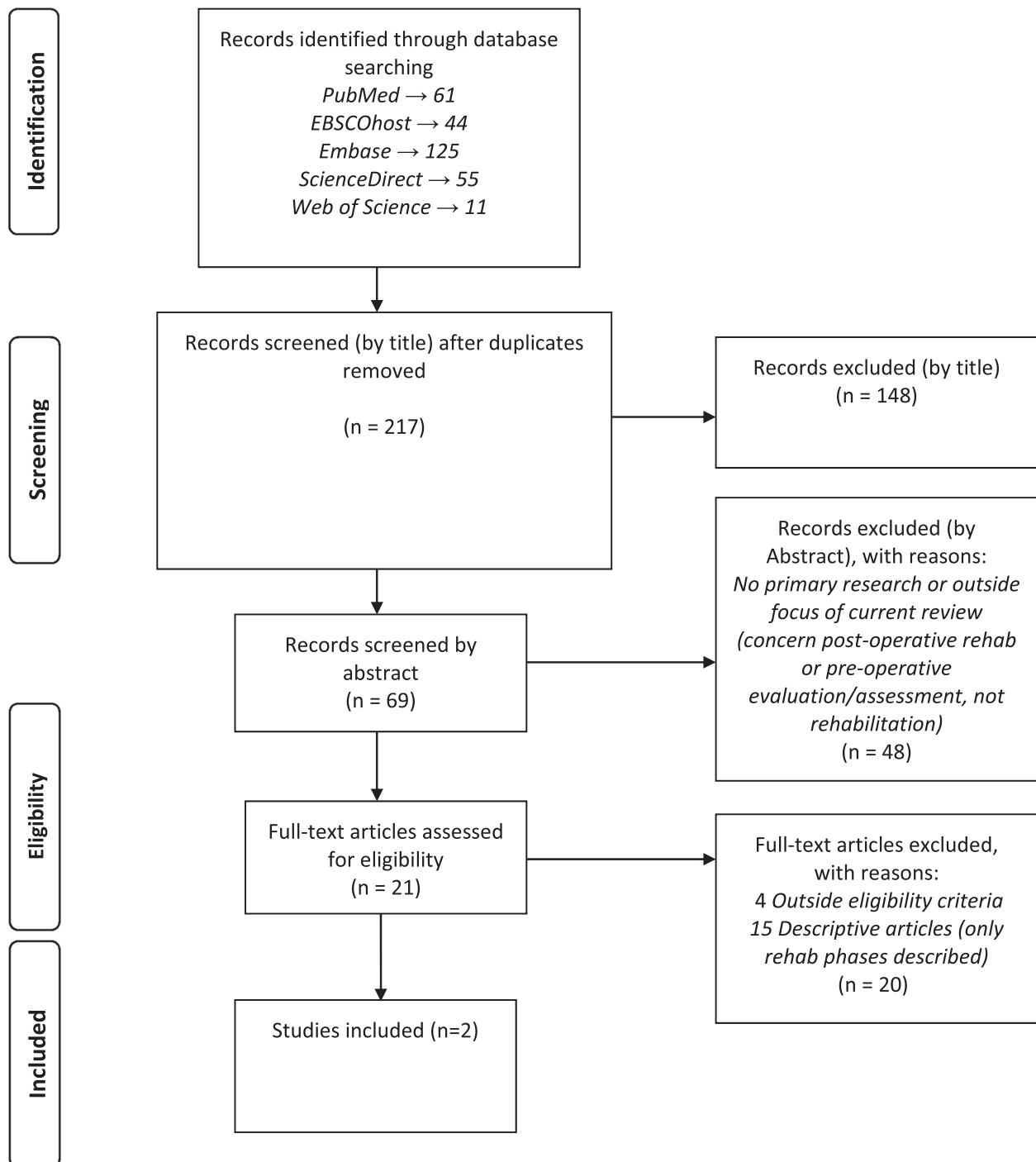


Fig. 1. PRISMA Flow Diagram of Literature Search.

Stanmore scale, meaning at least indoor walker with the use of walking aids) was achieved in 55 patients of all 87 (63%). They reported significantly better mobility in patients with unilateral BKA compared with a unilateral AKA (34/43 or 79% versus 10/27 or 37%, respectively; chi-square analysis,  $p = 0.001$ ). Mobility was not affected by any other factors, in particular, age, sex, diabetes, emergency admission, indication for amputation and previous vascular surgery, according to a univariate analysis. The LOS of the mobile and immobile patients was also recorded (median duration of stay was 45 versus 49 days), showing no significant differences.

#### Qualitative study

The study by Dekker et al. described a qualitative study with two explorative focus groups of in total 16 experts in the field of LLA and pre-operative rehabilitation.[18] The aim was to investigate the experiences of professionals and researchers in the field of LLA with the use of pre-rehabilitation in these patients. Also the opinions of the experts regarding need and feasibility of such a pre-rehabilitation program was assessed. The panel of experts consisted of highly qualified and experienced medical professionals and researchers in the field of



**Table 1**  
Risk of Bias Assessment in Individual Study using Cochrane Risk of Bias Tool for NRSI

Domain	Assessment by Outcome(study of Turney et al.[32])	Comment
<i>Bias due to confounding</i>	Serious risk of bias;	No adjustment for confounders;
<i>Bias in selection of participants into the study</i>	Moderate risk of bias;	Selection into the study related to an effect of both intervention and outcome;
<i>Bias in measurement of interventions</i>	No information on which to base a judgement about risk of bias for this domain;	No definition and explanation of intervention;
<i>Bias due to departures from intended interventions</i>	No information on which to base a judgement about risk of bias for this domain;	No information is reported on whether there is departure from the intended intervention;
<i>Bias due to missing data</i>	No information on which to base a judgement about risk of bias for this domain;	No information is reported about missing data or the potential for data to be missing;
<i>Bias in measurement of outcomes</i>	Serious risk of bias;	The outcome measure was subjective (i.e. likely to be influenced by knowledge of the intervention received by study participants) and was assessed by outcome assessors aware of the intervention received by study participants;
<i>Bias in selection of the reported result</i>	No information on which to base a judgement about risk of bias for this domain;	There is too little information to make a judgement. No statistical analysis of the results provided in the article.

vascular surgery, rehabilitation medicine, physiotherapy, psychology, occupational therapy and movement sciences. The study showed that hardly any professional in the Northern Netherlands had experiences with pre-operative rehabilitation in dysvascular patients awaiting an amputation.[18] Although the experts saw the potential importance, benefits, and effectiveness of a pre-rehabilitation program for dysvascular LLA, they had strong doubts about the feasibility of such a program. These patients were described as difficult group for pre-operative rehabilitation due to short time window prior to surgery, older age, and multiple co-morbidities. Also motivation in this group was thought to be poor, resulting in small chances of a behavioral change. A pre-operative rehabilitation program seemed only possible for a selected subgroup of younger dysvascular patients, with a relatively large window of time before the elected surgery.[18]

## Discussion

The aim of this study was to test the hypothesis that given the positive effects of post-surgical outcomes in many patient populations, pre-operative rehabilitation will improve post-operative outcomes, like physical functioning, mobility, LOS and recovery time, HRQoL, and complication rates, in LLA. A systematic literature search was performed to test this hypothesis. In literature only one quantitative study investigated the effects of a pre-operative rehabilitation program for LAA patients and one qualitative study investigated the need and feasibility of a pre-operative program for LLA. The effects on post-operative mobility of these patients was assessed using the Wood/Stanmore mobility scale.[35] The outcomes of the study showed improved patient mobility in patients with unilateral BKA compared to unilateral AKA patients. No association was found between mobility and age, sex, diabetes mellitus, amputation cause and previous vascular surgery. In the included qualitative study it was concluded that pre-operative rehabilitation seems only possible for a selected subgroup of younger dysvascular patients, with a relatively large window of time before the elected surgery.

## Significance of results

In the study of Turney et al. 63% LLA patients reached at least indoor mobility with the use of assisted devices, [35] which is much more than the portion of patient reaching this level of mobility described in a previous study (10–15%).[37] This result was attributed to the in-patient-based rehabilitation program which was offered to the LLA patients on a daily basis prior to their operation, and continued daily until discharge. No control group was included however, making it hard to

weigh this outcome.

A clear association between the applied pre-operative physiotherapy and the improved mobility of the patients after their operation has not been presented in this study. This could mean that other factors other than the pre-rehabilitation physical exercises could have also contributed to the high numbers of post-operative mobility of the patients, including, for instance, high selectivity of patients with relatively better and more stable pre-operative physical condition compared to previous literature. This may well result in exclusion of patients with significant comorbid diseases who might, in fact, represent a population group that would benefit most from pre-operative physiotherapy due to greater physical deconditioning and poorer health status.

In the paper of Dekker et al. a study was described where two focus groups were held with a multidisciplinary group of clinicians and researchers in the field of amputation and pre-operative rehabilitation. [18] It was concluded that a pre-operative rehabilitation program seems only feasible in a selected subgroup of younger dysvascular patients.

## Methodological issues

Despite the promising mobility outcomes described by Turney et al., several issues arise with respect to the methodological set up of the study.[35] Firstly, the quality assessment applied for this study showed poor methodological quality based on poor scorings on several quality items among which “unclearly defined exposure measures” and “lack of measurement of possible confounding variables” (Appendix 2). The systematic review of Sansam et al.,[38] which investigated factors predicting the walking ability following LLA, also assessed the quality of the study by Turney et al.,[35] and confirms our conclusion that the study is of poor methodological quality. Sansam et al. have based their quality assessment on the rating method from the UK National Service Framework for Long-term Conditions,[39] which has face validity and allows assessment of quality in non-randomized cohort studies.

Secondly, the exact components of the in-patient rehabilitation program, such as the specific physical exercises, frequency of therapy sessions and their duration, as well as the duration of the whole therapy (in days/weeks) prior to amputation, were not described in the article. This poses various difficulties in terms of reproducibility and raises doubts about the validity and reliability of the results stated in the article. Also the poor description of the content of the intervention increases the risk of bias of the study. The poor methodological quality and high risk of bias prevent any definitive conclusions about the post-operative outcomes examined.

**Table 2**  
General study information

General Study Information								
Author(year of publication)	Duration of study (years)	Total number of patients (N)	Patient population	Post-operative outcome	Outcome measurement tool	Type of pre-operative intervention	Components of intervention (Frequency IntensityDuration)	Inclusion/Exclusion criteria
Turney et al. (2001)	2	87	Major LLA	Mobility	Wood/Stannmore mobility scale	Physiotherapy and rehabilitation	Daily physiotherapyNo information on exact exercises, intensity, orduration	Inclusion: patients with any mobility/any potential for mobility before amputation

**Table 3**  
Study characteristics

Studies		Patient Characteristics							
Author	Number of patients (N)	Enrolled number amputation patients	Final number of patients (% drop-outs)	Median age participants (years)	Level of amputation(N of patients)	Reason for amputation (N of patients)	Male (%)	Female(%)	Mobile after amputation-N (% of all patients)
Turney et al. (2001)	87		66 (24)	74	Unilateral BKA (43)Unilateral AKA (27)Hip disarticulations (2)Bilateral amputation (15): - Bilateral BKA (11) - Bilateral AKA (2) - One BKA and one AKA (2)	Critical ischemia (70)Orthopedic, ulcerative, and oncological reasons (17)	60(69)	27(31)	55 (63)

Abbreviations: AKA = Above Knee Amputation; BKA = Below Knee Amputation

## Limitations of the current study

Several limitations of this study to test our hypothesis require further elaboration. First, English-language restriction was applied during the study selection phases, which may introduce a language bias and lead to erroneous conclusions. Moreover, the exclusive reliance on English-language studies may not represent all of the evidence.

Another very important limitation was the lack of studies available on the researched topic. The fact that only two studies from our literature search of five databases fulfilled the eligibility criteria for inclusion is a clear indication of the scarcity of research in the field of pre-operative rehabilitation for LLA patients. These limited results make it impossible to support or reject our hypothesis, but, on the other hand, stimulated our interest in the investigation of pre-rehabilitation practices for LAA patients and the possibilities of testing their effectiveness on post-operative patient outcomes even further.

As shown by this study, the influence of pre-operative rehabilitation program involving physical exercises on post-operative outcomes of LLA patients has received too little attention in the literature. For the achievement of optimal results after the amputation in terms of physical and psychological functioning and well-being, as well as satisfactory quality of life, insight is needed into the effectiveness and feasibility of such a pre-rehabilitation program. Therefore it is necessary to study a complete cohort of LLA patients prospectively with respect to their pre- and post-operative conditioning, in order to compare the outcomes of patients who received pre-operative therapy with those of no-intervention patients.

As shown in the included qualitative study, it should be mentioned that the expert opinion of a multidisciplinary group in The Netherlands is that pre-operative rehabilitation is only suitable for a selected group of relatively young dysvascular patients.[18] This poor suitability could be the reason for the lack of literature available on this topic. Though it

is reported that 13.6% of LLA patients received preoperative physical or occupational therapy between 2005 and 2010 through VA in the USA, showing that there is potential for such a program in a selected group. [40]

## Conclusions and future work

Based on the current literature the hypothesis that given the positive effects of post-surgical outcomes in many patient populations, pre-operative rehabilitation will improve post-operative outcomes after LLA could not be supported nor rejected. It seems however, that a pre-operative rehabilitation program might only be feasible in a selected subgroup of relatively young dysvascular patients. The results point to the conclusion that future research is still needed to understand the potential benefit of pre-operative rehabilitation input in LLA patients. The possibility of developing and clinically implementing a pre-operative rehabilitation program has the potential to benefit patients who might well be in need of a better pre-operative treatment and preparation for the post-operative period and its hardships. It has been shown that there is significant lack of information in the literature on pre-rehabilitation of patients scheduled for LLA and its effect on post-operative patient outcomes. Future clinical trials are required to define the role, nature, duration, intensity, and frequency of pre-operative exercise training in the management of a selected group of relatively young dysvascular patients who are to undergo LLA.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix

### Appendix 1: Search strategies and databases searched

EBSCOhost  
TX (preoperative OR pre-operative) AND TX rehabilitation AND TX lower limb AND TX amput\*.  
PubMed  
("Preoperative Care"[Mesh] OR preoperative care[tw] OR preoperative service\*[tw] OR preoperative program\*[tw] OR preoperative intervention\*[tw] OR preoperative training[tw] OR preoperative exercise[tw] OR preoperative physical activity[tw] OR preoperative therap\*[tw] OR preoperative rehabil\*[tw] OR pre-operative care[tw] OR pre-operative program\*[tw] OR pre-operative intervention\*[tw] OR pre-operative training[tw] OR pre-operative exercise[tw] OR pre-operative physical activity[tw] OR pre-operative therap\*[tw] OR pre-operative rehabil\*[tw] OR pre-operative service\*[tw]) AND ((physical activity OR fitness) OR ("rehabilitation"[Subheading] OR rehabilitat\*[tw] OR prehabilitat\*[tw] OR pre-rehabilitat\*[tw])) AND ("Amputation"[Mesh] OR amputat\*[tw] OR amput\*[tw]).  
EMBASE  
'preoperative' OR 'pre-operative' AND ('rehabilitation'/exp OR rehabilitation) AND lower AND ('limb' OR 'limb'/exp OR limb OR 'extremity'/exp OR 'extremity') AND ('amputation' OR 'amputation'/exp OR amputation OR 'amputee'/exp OR 'amputee')  
ScienceDirect  
TITLE-ABSTR-KEY((preoperative OR pre-operative) rehabilitation ) and TITLE-ABSTR-KEY(lower amput\*)[All Sources(Medicine and Dentistry)].  
Web of Science  
((TS=(lower limb OR lower extremity amput\*) AND TI=(preoperative OR pre-operative) AND TI=(rehabilitation OR physical therapy OR physical activity OR intervention OR service OR program\* OR exercise OR prehabilitation OR prerehabilitation OR fitness))) AND LANGUAGE: (English) AND DOCUMENT TYPES: (Article)/  
Timespan: All years.

### Appendix 2

#### TableA2



**Table A2**

Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies Available from: <http://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardi-vascular-risk-reduction/tools/cohort.htm>.

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			
<b>Quality Rating (Good, Fair, or Poor) (see guidance)</b>			
Rater #1 initials:			
Rater #2 initials:			
Additional Comments (If POOR, please state why):			

\*CD, cannot determine; NA, not applicable; NR, not reported

## References

- [1] Bragaru M, Dekker R, Geertzen JH, Dijkstra PU. Amputees and sports: a systematic review. *Sports Med*. 2011;41(9):721–40.
- [2] Dillingham TR, Pezzin LE, MacKenzie EJ. Limb amputation and limb deficiency: epidemiology and recent trends in the United States. *South Med J*. 2002;95(8):875–83.
- [3] Andrews L, Anderson L, Fairbairn S, Downing L. Care planning for children with lower limb amputation. *Nurs. Child. Young People*. 2012;24(1):14–9.
- [4] Abou-Zamzam Jr AM, Teruya TH, Killeen JD, Ballard JL. Major lower extremity amputation in an academic vascular center. *Ann Vasc Surg*. 2003 Jan;17(1):86–90.
- [5] Guidelines amputation and prosthetics of the lower extremity. Dutch Society for of Rehabilitation Medicine. Oct 2012. Available from: : <https://richtlijnendatabase.nl/> [access date 22-06-2020].
- [6] Stineman MG, Kwong PL, Xie D, Kurichi JE, Ripley DC, Brooks DM, et al. Prognostic differences for functional recovery after major lower limb amputation: effects of the timing and type of inpatient rehabilitation services in the Veterans Health Administration. *PM R*. 2010;2(4):232–43.
- [7] Chin T, Sawamura S, Fujita H, Nakajima S, Oyabu H, Nagakura Y, et al. Physical fitness of lower limb amputees. *Am J Phys Med Rehabil*. 2002;81(5):321–5.
- [8] Pernot HF, de Witte LP, Lindeman E, Cluitmans J. Daily functioning of the lower extremity amputee: an overview of the literature. *Clin Rehabil*. 1997;11(2):93–106.
- [9] Santa Mina D, Clarke H, Ritvo P, Leung YW, Matthew AG, Katz J, Trachtenberg J, Alibhai SM. Effect of total-body prehabilitation on postoperative outcomes: a systematic review and meta-analysis. *Physiotherapy*. 2013. pii: S0031-9406(13)00114-4.
- [10] Berkel AEM, Bongers BC, van Kamp MS, Kotte H, Heltevredn P, de Jongh FHC, et al. The effects of prehabilitation versus usual care to reduce postoperative complications in high-risk patients with colorectal cancer or dysplasia scheduled for elective colorectal resection: study protocol of a randomized controlled trial. *BMC Gastroenterol*. 2018;18(1):29.
- [11] Ditmyer MM, Topp R, Pifer M. Prehabilitation in preparation for orthopaedic surgery. *Orthop Nurs* 2002; 21(5):43–51; quiz 52–4.
- [12] Vitali M, Redhead RG. The modern concept of the general management of amputee rehabilitation including immediate post-operative fitting. *Ann R Coll Surg Engl* 1967;40(4):251–60.
- [13] Coudeyre E, Jardin C, Givron P, Ribnik P, Revel M, Rannou F. Could preoperative rehabilitation modify postoperative outcomes after total hip and knee arthroplasty? Elaboration of French clinical practice guidelines. *Ann Readapt Med Phys* 2007;50(3):189–97.
- [14] Esquenazi A, Meier 3rd. RH. Rehabilitation in limb deficiency. 4. Limb amputation. *Arch Phys Med Rehabil* 1996;77(3 Suppl):S18–28.
- [15] Knetsche RP, Leopold SS, Brage ME. Inpatient management of lower extremity amputations. *Foot Ankle Clin*. 2001;6(2):229–41.
- [16] Pandian G, Kowalske K. Daily functioning of patients with an amputated lower extremity. *Clin Orthop Relat Res*. 1999;361:91–7.
- [17] Engstrand JL. Rehabilitation of the patient with a lower extremity amputation. *Nurs Clin North Am*. 1976;11(4):659–69.
- [18] Dekker R, Hristova YV, Hijmans JM, Geertzen JHB. Pre-operative rehabilitation for dysvascular lower-limb amputee patients: A focus group study involving medical professionals. *PLoS ONE* 2018;13(10):e0204726.
- [19] US Department of Veterans Affairs. VA/DoD Clinical Practice Guideline for Rehabilitation of Individuals with Lower Limb Amputation. Sept 2017 Available at: <http://www.healthquality.va.gov/guidelines/Rehab/amp/>. [access date 22-06-2020].
- [20] Arthur HM, Daniels C, McKelvie R, Hirsh J, Rush B. Effect of a preoperative intervention on preoperative and postoperative outcomes in low-risk patients awaiting elective coronary artery bypass graft surgery. A randomized, controlled trial. *Ann Intern Med*. 2000;133(4):253–62.
- [21] Hulzebos EH, Smit Y, Helden PP, van Meeteren NL. Preoperative physical therapy for elective cardiac surgery patients. *Cochrane Database Syst Rev*. 2012; 11:CD010118.
- [22] Weiner P, Zeidan F, Zamir D, Pelled B, Waizman J, Beckerman M, et al. Prophylactic inspiratory muscle training in patients undergoing coronary artery bypass graft. *World J Surg* 1998;22(5):427–31.
- [23] Rosenfeldt F, Braun L, Spitzer O, Bradley S, Shepherd J, Bailey M, et al. Physical conditioning and mental stress reduction—a randomised trial in patients undergoing cardiac surgery. *BMC Complement Altern Med* 2011;9(11):20.
- [24] Bäck M, Wennerblom B, Wittboldt S, Cider A. Effects of high frequency exercise in patients before and after elective percutaneous coronary intervention. *Eur J Cardiovasc Nurs* 2008 Dec;7(4):307–13.
- [25] Dronkers JJ, Lamberts H, Reutelingsperger IM, Naber RH, Dronkers-Landman CM, Veldman A, et al. Preoperative therapeutic programme for elderly patients scheduled for elective abdominal oncological surgery: a randomized controlled pilot study. *Clin Rehabil*. 2010 Jul;24(7):614–22.
- [26] Valkenet K, van de Port IG, Dronkers JJ, de Vries WR, Lindeman E, Backx FJ. The effects of preoperative exercise therapy on postoperative outcome: a systematic review. *Clin Rehabil*. 2011;25(2):99–111.
- [27] Silkman Baker C, McKeon JM. Does preoperative rehabilitation improve patient-based outcomes in persons who have undergone total knee arthroplasty? A systematic review. *PM R* 2012;4(10):756–67.
- [28] Morano MT, Araújo AS, Nascimento FB, da Silva GF, Mesquita R, Pinto JS, et al. Preoperative pulmonary rehabilitation versus chest physical therapy in patients undergoing lung cancer resection: a pilot randomized controlled trial. *Arch Phys Med Rehabil* 2013;94(1):53–8.
- [29] Li X, Li S, Yan S, Wang Y, Wang X, Sihoe ADL, et al. Impact of preoperative exercise therapy on surgical outcomes in lung cancer patients with or without COPD: a systematic review and meta-analysis. *Cancer Manag Res* 2019;20(11):1765–77.
- [30] Wiesinger GF, Quittan M, Zimmermann K, Nuhr M, Wichlas M, Bodingbauer M, et al. Physical performance and health-related quality of life in men on a liver transplantation waiting list. *J Rehabil Med* 2001;33(6):260–5.
- [31] Turner DA, Cheifetz IM, Rehder KJ, Williford WL, Bonadonna D, Banuelos SJ, et al. Active rehabilitation and physical therapy during extracorporeal membrane oxygenation while awaiting lung transplantation: a practical approach. *Crit Care Med* 2011;39(12):2593–8.
- [32] Rochester CL. Pulmonary rehabilitation for patients who undergo lung-volume-reduction surgery or lung transplantation. *Respir Care*. 2008;53(9):1196–202.
- [33] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *PLoS Med* 6(7), 2009; e1000100.

- [34] Sterne JAC, Higgins JPT, Reeves BC on behalf of the development group for ACROBAT-NRSI. A Cochrane Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI), Version 1.0.0, 24 September 2014. Available from <http://www.bristol.ac.uk/population-health-sciences/centres/cre-syda/barr/riskofbias/robins-i/acrobat-nrsi/> [accessed 22-6-2020].
- [35] Turney BW, Kent SJ, Walker RT, Loftus IM. Amputations: no longer the end of the road. *J R Coll Surg Edinb* 2001;46(5):271–3.
- [36] Davies B, Datta D. Mobility outcome following unilateral lower limb amputation. *Prosthet Orthot Int* 2003;27(3):186–90.
- [37] Houghton AD, Taylor PR, Thurlow S, Rootes E, McColl I. Success rates for rehabilitation of vascular amputees: implications for preoperative assessment and amputation level. *Br J Surg* 1992;79:753–5.
- [38] Sansam K, Neumann V, O'Connor R, Bhakta B. Predicting walking ability following lower limb amputation: a systematic review of the literature. *J Rehabil Med* 2009;41(8):593–603.
- [39] Department of Health Long-term Conditions NSF Team. The National Service Framework for Long-term Conditions: Annex 2 Research and evidence. UK: Department of Health; 2005, p. 88.
- [40] Resnik LJ, Borgia ML. Factors associated with utilization of preoperative and postoperative rehabilitation services by patients with amputation in the VA system: an observational study. *Phys Ther* 2013;93:1197–210.